the effectiveness of physical activity. The presence in patients with obesity and overweight polymorphisms of genes that adversely affect carbohydrate and fat metabolism, dictates the need to organize a special personalized approach to diet therapy and exercise.

P291 NEPHROGENIC DIABETES INSIPIDUS IN A FEMALE INFANT

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Aim Nephrogenic Diabetes Insipidus (NDI) is rare. 90% of cases are due to a defect in the AVPR2 gene which is widely believed to be inherited in an X-linked recessive pattern; from asymptomatic carrier mothers, to severely affected sons, but not daughters. Other, less common cases (~1% of NDI cases), are inherited in an autosomal dominant pattern due to a defect in the AQP2 gene. However, our case will demonstrate how females can present with symptomatic NDI secondary to AVPR2 mutation.

Methods This is a case study of a 14-month-old girl who was referred to the Paediatric Outpatient Department with a history of faltering growth, excessive drinking and plentiful wet nappies. At birth she plotted on the 50th centile for weight but subsequently dropped to the 9th. Weaning was a difficult, with her preferring liquids to solids. Moreover, excessive thirst resulted in her drinking water from the swimming pool, bath water and even the dog's bowl. Serum electrolytes, in addition to serum and urine osmolality and a desmopressin test, confirmed the diagnosis of NDI.

There was positive family history with the patient's Father having NDI, treated initially with diuretics then desmopressin until age 14, and since no longer requiring medication. An assumption was made that the patient thus acquired NDI via autosomal dominant inheritance of AQP2 gene. However, genetic tests were not performed at this stage.

Results The patient's Father was found to be hemizygous for AVPR2 gene. Genetic testing then revealed the patient to be a carrier of AVPR2 gene. Inherited via X-linked recessive form this would not normally affect females. Nevertheless, due to lyonisation of X-chromosome this patient was symptomatic.

Conclusion X-linked autosomal recessive disorders can also affect females. This is due to the process of lyonisation, which in itself has different forms and causes. Appreciation of lyonisation defect is crucial in the diagnosis and family counselling of patients with X-linked recessive disorders such as NDI, in addition to other more common disorders such as Glucose-6-Phosphate Dehydrogenase Deficiency (G6PD), Duchenne Muscular Dystrophy or Haemophilia.

P292 NEONATAL DIABETES IN A TERTIARY CENTRE; GENETICS DICTATING MANAGEMENT

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Background Neonatal diabetes mellitus is a rare condition with one case per 300,000 to 500,000 live births. It presents with marked hyperglycaemia in the first six months of life and is commonly of generic origin. Approximately half of cases are transient (TNDM) with the remainder being permanent (PNDM). The majority of Permanent Diabetes Mellitus (PNDM) cases are secondary to genetic mutations in K-ATP channel genes.

Case We report two infants who presented in the neonatal period with hyperglycaemia and were subsequently diagnosed with neonatal diabetes.

The first infant presented at 22 hours of life with blood glucose of 44.3 mmol/L and in ketoacidosis. He was born by LSCS at 34 weeks gestation due to IUGR with a birth weight of 1.36 kg. He received an IV insulin infusion for two months with frequent dose titration due to challenging glycaemic control. He was then successfully transitioned to a subcutaneous insulin infusion pump. Genetic analysis confirmed homozygous INS non sense variant, p(Ar43Ter).

The second infant presented at six weeks of age in severe diabetic ketoacidosis with a blood glucose of 60 mmol/L. She was born at term weighing 2.46 kg following induction of labour for IUGR. She presented with lethargy and vomiting for 24 hours on a background of failure to thrive and chronic candidiasis from birth. She was managed with an IV insulin infusion in the ICU before transitioning to a subcutaneous insulin pump. Genetic analysis revealed a *de novo* KCNJ11 gene mutation. She was then successfully transitioned to oral Glibenclamide which optimised her glycaemic control and resulted in complete withdrawal of subcutaneous insulin.

Discussion These are two cases of NDM with identified genetic mutations. The INS mutation is localised to amino acid residues affecting cleavage and/or folding of pre-proinsulin and pro-insulin which leads to prolonged ER stress and subsequent B-cell apoptosis. The KCNJ11 gene mutation identified in our second patient results in K-ATP channel overactivity. The K-ATP channel is at the end of the glycolytic pathway and has a KIR amino terminus responsible for channel gating. Its deletion results in channels that are continuously closed reducing sensitivity to inhibitory ATP and resulting in dramatic hyperglycaemia. Oral glibenclamide inhibits K-ATP channel activity with resultant normoglycaemia. Early identification is essential for optimal management and targeted therapy.

P293 AN AUDIT OF PREGNANCY OUTCOMES IN WOMEN WITH CHILDHOOD ONSET TYPE 1 DIABETES MELLITUS

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Background Pregnancy in women with type 1 diabetes mellitus is associated with an increased risk of congenital malformations, obstetric complications, and neonatal morbidity. In order to minimise morbidity for both mothers and infants there needs to be good interdisciplinary care between diabetologists, obstetricians, neonatologists and relevant nursing specialists.